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| 10/697,599 | 10/29/2003 | Austin L. Gurney | 39766-0125A | 7558 |

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| EXAMINER | |
|---|---|
| HISSONG, BRUCE D | |
| **ART UNIT** | **PAPER NUMBER** |
| 1646 | |

DATE MAILED: 03/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/697,599 | GURNEY, AUSTIN L. | |
| | Examiner | Art Unit | |
| | Bruce D. Hissong, Ph.D. | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *1-13 and 29-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-49* are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 October 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/18/05, 1/25/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *PTO-948*.

## DETAILED ACTION

***Election/Restrictions***

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-13, drawn to a method for inhibiting interleukin-17 (IL-17) production by T cells, classified in class 514, subclass 2.

II. Claims 14-28, drawn to a method for the treatment of an inflammatory disease, classified in class 424, subclass 130.1.

III. Claims 29-37, drawn to a method for identifying an anti-inflammatory agent, classified in class 436, subclass 536.

IV. Claims 38-49, drawn to a method for inducing IL-17 production in a mammalian subject, classified in class 514, subclass 2.

The inventions are distinct, each from the other because of the following reasons:

Inventions I-IV are independent and distinct inventions, each from the other, because the methods are practiced with materially different process steps for materially different purposes, and each method requires a non-coextensive search because of different starting materials, process steps, and goals. The inventions of groups I and IV are drawn to methods of inhibiting or inducing IL-17 production, respectively, and thus have different starting materials (an inhibitor/antagonist vs a stimulator/agonist), and different goals. The invention of group II is drawn to methods of treating specific diseases, and thus has different process steps and different goals than the inventions of groups I, III, and IV. Group III is drawn to an in vitro method for identifying an anti-inflammatory agent, and thus has different starting materials, process steps, and goals than the method of treating a disease of group II, or the methods of inhibiting or inducing production of IL-17 of groups I and IV.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

During a telephone conversation with Ginger Dreger on 1/23/2006 a provisional election was made with traverse to prosecute the invention of Group II, claims 14-28. Affirmation of this election and presentation of grounds for traversal must be made by applicant in replying to this Office action. Claims 1-13 and 29-49 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

***Priority***

The instant application claims benefit of provisional application 60/423,090, filed on 10/30/2002, which has been determined to be the earliest effective filing date of the instant application.

***Information Disclosure Statement***

1. The information disclosure statement received on 1/18/2005 has been fully considered by the Examiner.

2. The information disclosure statement received on 1/25/2006 has been fully considered by the Examiner.

***Specification:***

The use of the following trademarks has been noted in this application: Sepharose (p. 17, paragraph 0056) and FLAG (p. 26, paragraph 0088, and p. 27, paragraph 0091, Robocycler (p. 31, paragraph 0104), Epics-XL (p. 31, paragraph 0105), and MoFlo (p. 32, paragraph 0106). Trademarks should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the

proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

***Claim Rejections - 35 USC § 112, first paragraph - enablement***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The factors to be considered when determining if the disclosure satisfies the enablement requirement have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breath of claims. Ex Parte Forman, (230 USPQ 546 (Bd. Pat. App. & Int. 1986); In re Wands, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

1. Claims 14-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating diseases characterized by delayed-type hypersensitivity, as described in Example 2, does not reasonably provide enablement for any other treatment of any other disease characterized by elevated expression of IL-17. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims of the instant application are drawn to methods of treating inflammatory disease characterized by elevated expression of IL-17. In particular, claim 16 is drawn to a number of inflammatory diseases to be treated by the claimed method. While the specification, on pages 1-2 and 22-23 recites diseases that are characterized by elevated IL-17 expression, the specification provides no guidance or working examples that teach that these, or any other disease, can be treated by administration of an IL-23 antagonist. Also, there is no guidance or examples in the specification showing that diseases such as Crohn's disease, ulcerative colitits, inflammatory bowel disease, Alzheimer's disease, and pyresis are associated with elevated IL-17 expression. The specification only shows an example showing that IL-23p19-deficient mice exhibit decreased delayed-type hypersensitivity reactions. Additionally, the data of Example 2

was obtained by decreasing IL-23 levels by genetic knock-out of the IL-23019 gene, and thus may not necessarily reflect pathological conditions in a genetically intact animal with inflammatory disease. Because inflammatory disease development and progression is often a complex process involving many factors, a person of ordinary skill in the art would not be able to predict, without further, undue experimentation, which diseases could be treated by decreasing IL-23 expression. Furthermore, the data presented in Example 2 was not generated by administration of any IL-23 antagonist, and the skilled artisan would also require further, undue experimentation, to determine which diseases could be treated by administration of an IL-23 antagonist.

In summary, due to the breadth of the claims, which read on any disease characterized by increased IL-17 expression, the lack of guidance or examples in the specification that show that any particular disease, other than those characterized by delayed-type hypersensitivity, can be treated by decreasing IL-23 levels, and the unpredictability of the art regarding which diseases could be treated with an IL-23 antagonist, a person of ordinary skill in the art would require further, undue experimentation to use the claimed invention commensurate in scope with the claims.

2. Claims 14-18 and 26-28, as well as dependent claims 19-25, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for IL-23 antagonists that are anti-IL-23 antibodies or anti-IL23 receptor antibodies, does not reasonably provide enablement for any other IL-23 antagonist. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims are drawn to the administration of IL-23 antagonists for the treatment of disease. The breadth of the claims is excessive because the claims read on any molecule, with no limitations on structure of chemical type, that can function as an IL-23 antagonist. Although the specification teaches anti-IL-23 antibodies and anti-IL-23 receptor antibodies, the specification does not provide any guidance or working examples of any other potential IL-23 antagonist. Such antagonists could potentially include blocking peptides, peptide mimetics, and soluble receptors, as well as chemical compounds, and siRNA or antisense RNA molecules. The specification does not teach how to make or use any other IL-23 antagonist other than anti-IL-23 antibodies or anti-IL-23 receptor antibodies. A person of ordinary skill in the art would not be able to predict how to design and

make any peptide inhibitor, mimetic, or chemical inhibitor that would function as an IL-23 inhibitor, and would require further, excessive experimentation to determine how to make such molecules, and to test the molecules for the desired activity.

In summary, due to the excessive breadth of the claims, which read on any potential molecule which can act as an IL-23 antagonist, the lack of guidance and working examples in the specification that teach any molecules other than anti-IL23 and anti-IL23 receptor antibodies, and the unpredictability in the art regarding how to make and test for IL-23 antagonist molecules, a person of ordinary skill in the art would not be able to use any molecule, other than anti-IL23 or anti-IL23 receptor antibodies, commensurate in scope with the claims without further, undue experimentation. Claims 19-25 are rejected for depending from rejected base claims.

3. Claim 20, and dependent claim 21, is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Fv, Fab, Fab', or $F(ab')_2$ antibody fragments, does not reasonably provide enablement for any other antibody fragment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The breadth of claim 20 is excessively broad because, given the broadest possible interpretation, the claim reads on any potential antibody fragment. The specification teaches antibody fragments such as Fv, Fab, Fab', and $F(ab')_2$ fragments, which a skilled artisan would be familiar with, but does not teach any other antibody fragment that could be used, and provides no guidance or working examples at all of any antibody fragment that could act as an IL-23 antagonist. A person of ordinary skill in the art, therefore, would not be able to predict which of the many possible fragments of an anti-IL-23 antibody could act as antagonists of IL-23.

In summary, due to the excessive breadth of the claim, which reads on any potential antibody fragment, the lack of teachings or examples in the specification that teach that antibody fragment other than those discussed above, the unpredictability of the art regarding potential antibody fragments, a skilled artisan would require further, undue experimentation to determine which antibody fragments could be used commensurate in scope with the claims. Claim 21 is rejected for depending from claim 20.

***Claim Rejections - 35 USC § 112, first paragraph – written description***

Claims 14-18 and 26-28, as well as dependent claims 19-25, are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to antagonists of IL-23, including anti-IL-23 antibodies and anti-IL-23 receptor antibodies. The claims do not require the IL-23 antagonists of the instant invention to have any particular structure, and only require that they are able to antagonize or inhibit the action of IL-23. The claims read on any potential molecule that is capable of inhibiting or antagonizing IL-23, and in additional to any anti-IL-23 or anti-IL23 receptor antibody, could conceivably include small peptide molecules, peptide mimetics, soluble receptors, and chemical inhibitors. Thus, Applicants have not defined the genus of molecules that define IL-23 antagonists.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a requirement of IL-23 antagonism or inhibition. There is no identification of any particular portion of any potential molecule, such as an antibody fragment, that must be conserved in order to maintain function. Accordingly, in the absence of sufficient distinguishing characteristics, the specification does not provide adequate written description of the claimed genus.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of

the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only anti-IL-23 or anti-IL-23 receptor antibodies that are known in the art, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 19-25 are rejected for depending from rejected base claims.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 14-28 are rejected under 35 U.S.C. 102(e) as being anticipated by Chirica *et al* (US 6,756,481). The claims of the instant application are drawn to a method for treatment of an inflammatory disease characterized by expression of IL-17, comprising administering an antagonist of IL-23. Chirica *et al* disclose a receptor, termed DCRS5, for the polypeptide ligand IL-B30 (column 2, lines 34-48). Although Chirica *et al* use the terminology IL-B30 and DCRS5, Kastelein et al (US20050287593), on p. 6, paragraph 0045, teach that the polypeptide known as IL-B30 is the p19 subunit of IL-23; therefore, the IL-B30 of Chirica *et al* is in reality IL-23p19, and its receptor, DCRS5, is the IL-23 receptor subunit polypeptide that pairs with the IL-12Rβ1 subunit to form the IL-23 receptor.

Chirica *et al* anticipates the claims of the instant application for the following reasons. Chirica *et al* teach the IL-23 receptor subunit (identified as DCRS5 and SEQ ID NO:2 in Chirica

*et al*), and specifically teach antibodies and other binding compounds which specifically bind DCRS5/IL-23R, including antibodies in their native (i.e. full-length) form, and antibody fragments such as Fv, Fab, or Fab2 fragments (column 23, line 38 – column 24, line 5, and column 3, line 64 – column 4, line 10). Also taught by Chirica *et al* are anti-IL-23 antibodies of human origin (column 24, lines 34-36), and chimeric or humanized anti-DCRS5/IL-23R antibodies (column 24, lines 65-67). Thus, Chirica et al meets the limitations of claims 19-25 of the instant application.

Chirica *et al* also meets the limitations of claims 14-18 of the instant application by teaching that the DCRS5/IL-23R antagonists can be used to treat a number of conditions, including multiple sclerosis, psoriasis, and rheumatoid arthritis (column 29 line 62 – column 30, line 21, and column 31, lines 36-42), all of which are disclosed in the instant application as disorders associated with increased IL-17 expression. Chirica *et al* also teach co-administration of additional therapeutic agents, including anti-inflammatory agents or immunosuppresants (column 30, lines 10-14), including steroids (column 29, lines 62-64), which meets the limitations of claims 26-28 of the instant application.

Finally, it is noted that Kastelein *et al* is not being used as a grounds for rejection, but to provide evidence that the DCRS5 of Chirica *et al* is an alternative name for the IL-23 receptor subunit.

***Conclusion***

No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, Ph.D., can be reached at (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

BDH
Art Unit 1646

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PRIMARY EXAMINER